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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/673,617	01/25/2001	Kim Sorensen	030307/0191	2002

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FOLEY AND LARDNER
SUITE 500
3000 K STREET NW
WASHINGTON, DC 20007

EXAMINER

LEFFERS JR, GERALD G

ART UNIT PAPER NUMBER

1636

DATE MAILED: 06/30/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/673,617

Applicant(s)

SORENSEN ET AL.

Examiner

Gerald G Leffers Jr., PhD

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 23 January 2002.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-40 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-40 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☒ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| Paper No(s)/Mail Date <u>1/25/2001</u> . | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Claims 1-40 are pending in the instant application and are subject to the following examination on the merits.

Sequence Compliance

Receipt is acknowledged of a preliminary amendment in which a sequence listing, computer readable copy of the sequence listing (CRF) and attorney's statements concerning the sequence listing, filed 1/23/2002. These papers have been entered into the file and the application is now in sequence compliance.

Priority

Receipt is acknowledged of papers filed under 35 U.S.C. 119 (a)-(d) based on an application filed in Denmark on April 21, 1998 (Application No. 0551/98). Applicant has not complied with the requirements of 37 CFR 1.63(c), since the oath, declaration or application data sheet does not acknowledge the filing of any foreign application. A new oath, declaration or application data sheet is required in the body of which the present application should be identified by application number and filing date.

Acknowledgment is made of applicant's claim for foreign priority based on an application filed in Denmark on April 21, 1998 (Application No. 0551/98). It is noted, however, that applicant has not filed a certified copy of the foreign application as required by 35 U.S.C. 119(b).

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Information Disclosure Statement

Receipt is acknowledged of an information disclosure statement (IDS), filed 1/25/2001.

The signed and initialed PTO 1449 corresponding to the IDS has been mailed with this action.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-29, 31-40 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter that was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Each of the claims is directed to a recombinant vector comprising a gene coding for an amber suppressor that is a tRNA comprising the CUA anticodon and a replicon making the vector capable of replicating in a lactic acid bacterium. The vector must "consist essentially of" lactic acid bacterial DNA and must meet at least one of three very specific functional criteria:

- (i) when it is present in *L. lactis* strain FA4-1-1 having an amber mutation in the pyrF gene that is suppressible by the suppressor, it permits the strain to grow at 30°C at a doubling time of at most 100 minutes in a minimal medium not containing pyrimidine sources; or

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(ii) when it is present in a strain of *L. lactis* FH CY-1 that has an amber mutation in the *pyrF* gene, the amber mutation being suppressible by the suppressor, it permits the strain to acidify milk under identical conditions at essentially the same rate of that of the parent strain FH CY-1; or

(iii) it permits the *L. lactis* strain FA4-1-1 to grow at 30°C in a minimal medium not containing pyrimidine sources at a doubling time that is less than that for the *L. lactis* strain DN209 transformed with the vector pFG1.1, the pFG1.1 vector comprising a gene coding for a suppressor that is capable of suppressing the amber mutation in the DN209 strain, the transformed DN209 strain growing under conditions identical to those for the FA4-1-1 strain.

It is noted that while claim 15 is directed to specific embodiments of the claimed invention that are described in the instant specification, it is also directed to undefined “variants”, “mutants” and/or “derivatives” of these vectors. Thus, the rejected claims encompass a broad genus of replicons that must comprise a combination of elements (e.g. origin of replication controlling copy number of the vector in a given host cell, promoter and other regulatory sequences controlling the rate of transcription, suppressor gene encoding a tRNA comprising a CUA anticodon, etc.) that enable the replicon to meet very specific functional limitations with regard to doubling time and/or the ability to allow a specific transformed strain to acidify milk at the same rate as the corresponding untransformed strain.

The instant specification teaches the construction of two plasmid replicons, pFG100 and pFG200, that comprise a gene encoding an amber suppressor inserted into different *L. lactis* vector backbones (e.g. pIL2608 and pCT1138; see Examples 1 and 3). In each case the gene

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encoding supD from a known plasmid, pAK89 (Dickely, et al. Molecular Microbiology, Vol. 15, No. 5, pages 839-847, see Figure 3) was cloned into a *Lactococcus*-derived vector comprising different combinations of replicon elements yielding vectors having different functional characteristics. The specification does not, however, teach what are the structural/functional characteristics of the vectors described by the specification that necessarily meet the very specific functional requirements of the rejected claims. Therefore, there was no structural/functional basis provided by the specification for the skilled artisan to envision the combination of replicon/expression elements that would allow a given vector to meet the very specific functional limitations of the claims.

The prior art does not appear to describe what are the functional/structural requirements for a given construct to be able to meet the very specific functional requirements of the rejected claims. Therefore, given the broad genus of recombinant vectors embraced by the rejected claims and the very specific functional limitations of the claims, and given the fact that there is no structural/functional basis for the skilled artisan to envision additional vectors that meet the functional limitations of the claims, the skilled artisan would not have been able to envision a sufficient number of species embraced by the claims to describe the broadly claimed genus of such vectors. The skilled artisan would have reasonably concluded applicants were not in possession of the broadly claimed invention.

Claims 1-40 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter that was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which

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it is most nearly connected, to make and/or use the invention. **This is a biological deposit requirement.**

The application discloses plasmids and bacterial strains that are encompassed by the definitions for **biological material** set forth in 37 C.F.R. § 1.801. Because it is apparent that this biological material is essential for practicing the claimed invention, it must be obtainable by a reproducible method set forth in the specification or otherwise be known and readily available to the public as detailed in 37 C.F.R. §§ 1.801 through 1.809. These materials include the following:

- FA4-1-1 (DSM 12086)
- FH CY-1 (DSM 12087)
- CHCC4146 (DSM 12109)
- pFG1.1 (DSM 12088)
- pFG100 (DSM 12091)
- pFG200 (DSM 12108)
- DN209/pFG7/øvML3 (DSM 12089)

It is unclear whether this biological material is known and readily available to the public or that the written instructions are sufficient to reproducibly construct this biological material from starting materials known and readily available to the public. In addition, it is not clear that the starting materials and/or the plasmids and strains themselves will be available to the public for the duration of any patent term for claims issued from the instant claims. Accordingly, availability of such biological material is deemed necessary to satisfy the enablement provisions of 35 U.S.C. § 112. If this biological material is not obtainable or available, the requirements of 35 U.S.C. § 112 may be satisfied by a deposit of the biological material. In order for a deposit to meet all criteria set forth in 37 C.F.R. §§ 1.801-1.809, applicants or assignee must provide assurance of compliance with provisions of 37 C.F.R. §§ 1.801-1.809, in the form of a

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declaration or applicant's representative must provide a statement. **The content of such a declaration or statement is suggested by the enclosed attachment.** Because such deposit will not have been made prior to the effective filing date of the instant application, applicant is required to submit a verified statement from a person in a position to corroborate the fact, which states that the biological material which has been deposited is the biological material specifically identified in the application as filed (37 C.F.R. § 1.804). Such a statement need not be verified if the person is an agent or attorney registered to practice before the Office. Applicant is also reminded that the specification must contain reference to the deposit, including deposit (accession) number, date of deposit, name and address of the depository, and the complete taxonomic description.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter that the applicant regards as his invention.

Claims 1-40 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 is vague and indefinite in that the metes and bounds of the phrase “consisting essentially of lactic acid bacterial DNA” are unclear. The concept of “consisting essentially of” lactic acid bacterial DNA is not clearly defined in the specification. It is unclear what structural/functional characteristics of the recombinant vector can be altered and still have the vector satisfy the limitation of “consisting essentially of” lactic acid bacterial DNA. For example, could one introduce a gene encoding a selectable marker into the vector and meet the

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cited limitation so long as the gene has been codon-optimized for expression in a lactic acid bacterium, even if the selectable marker does not normally reside in such bacteria? It would be remedial to amend the claim to clearly indicate the structural/functional requirements that must be satisfied in order to meet the requirements of the limitation “consisting essentially of lactic acid bacterial DNA”.

The parenthetical use of the term “strain CHCC4146, DSM 12109” makes it unclear in part (ii) of claim 1 whether that particular strain of FH CY-1 must be used for the comparison of the functional properties of the claimed recombinant vector. Upon reading the specification, it appears that the comparison is in fact intended to be made using the DSM 12109 strain. It would be remedial to amend the claim language to clearly indicate whether one necessarily uses the DSM 12109 strain.

Claim 1, part (ii) is also vague and indefinite in that the metes and bounds of the phrase “essentially the same rate” are unclear. The term is not explicitly defined in the specification in such a way as to make it unambiguous as to how different the rates of acidification can be in order to be “essentially the same”. It would be remedial to amend the claim language to explicitly indicate what is meant by “essentially the same”.

Claims 4, 6, 10 and 20 recite the term “derived from”. It is unclear the nature and number of steps required in order to obtain a “derivative”. It would be remedial to amend the claims to indicate that the desired replicon or element is “obtained from” rather than “derived from”.

Claim 6 is vague and indefinite in that the metes and bounds of the “promoter not naturally related to the gene are unclear”. The specification does not clearly define the concept

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of a promoter being “not naturally related to” a given gene. It appears the phrase is intended to specify that the promoter is heterologous with regard to the gene and it would be remedial to amend the claim accordingly.

Claim 15 is vague and indefinite in that the metes and bounds of the phrase “said mutants, variants or derivatives essentially having the characteristics of the respective vector from which they are derived” are unclear. The specification does not clearly indicate which characteristics are to be evaluated with regard to being a “mutant”, “variant” or “derivative” of the two replicons, pFG100 and pFG200. Nor does the specification specify the degree of similarity for a given characteristic that must be met in order to satisfy the limitation of being a “mutant”, “variant” or “derivative” of the two replicons, pFG100 and pFG200. Therefore, it would be remedial to amend the claim language to delete the cited phrase and the terms “mutant”, “variant” and “derivative” as applied to pFG100 and pFG200.

Claim 16 is vague and indefinite in that it is unclear whether the claim further limits the vector of claim 1, which may already comprise a gene encoding a desired gene product. It would be remedial to amend the claim by inserting the word “further” prior to the term “comprises”.

Claim 18 is vague and indefinite in that there is no clear and positive prior antecedent basis for the term “the gene product” in claim 16, upon which claim 18 is dependent. After all, the recombinant vector of claim 1, upon which claim 16 is dependent, can encode multiple gene products.

Claim 20 recites that a gene product is “involved in” nisin synthesis or nisin resistance. How directly connected to these processes does the gene product have to be in order to be

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“involved in” the process? It would be remedial to more explicitly recite how the gene product is related to the synthesis or resistance to nisin.

Claims 32 and 33 are vague and indefinite in that they recite the term “pure culture”, which is subjective and not explicitly defined in the specification.

Claim 34 is vague and indefinite in that it recites the limitation of “105 colony forming units of the lactic acid bacterium per g”. The phrase is unclear in that it is unclear what is referred to by the letter “g”. It would be remedial to amend the claim to read “grams” and clearly indicate what is being weighed (e.g. grams of bacteria? food product?).

Claim 35 provides for the use of a recombinant vector composition as a starter culture, but, since the claim does not set forth any steps involved in the method/process, it is unclear what method/process applicant is intending to encompass. A claim is indefinite where it merely recites a use without any active, positive steps delimiting how this use is actually practiced.

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claim 35 is rejected under 35 U.S.C. 101 because the claimed recitation of a use, without setting forth any steps involved in the process, results in an improper definition of a process, i.e., results in a claim which is not a proper process claim under 35 U.S.C. 101. See for example *Ex parte Dunki*, 153 USPQ 678 (Bd.App. 1967) and *Clinical Products, Ltd. v. Brenner*, 255 F. Supp. 131, 149 USPQ 475 (D.D.C. 1966).

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Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Each of the claims is directed to a recombinant vector comprising a gene coding for an amber suppressor that is a tRNA comprising the CUA anticodon and a replicon making the vector capable of replicating in a lactic acid bacterium. The vector must “consist essentially of” lactic acid bacterial DNA and must meet at least one of three very specific functional criteria:

- (i) when it is present in *L. lactis* strain FA4-1-1 having an amber mutation in the *pyrF* gene that is suppressible by the suppressor, it permits the strain to grow at 30°C at a doubling time of at most 100 minutes in a minimal medium not containing pyrimidine sources; or
- (ii) when it is present in a strain of *L. lactis* FH CY-1 that has an amber mutation in the *pyrF* gene, the amber mutation being suppressible by the suppressor, it permits the strain to acidify milk under identical conditions at essentially the same rate of that of the parent strain FH CY-1; or
- (iii) it permits the *L. lactis* strain FA4-1-1 to grow at 30°C in a minimal medium not containing pyrimidine sources at a doubling time that is less than that for the *L. lactis* strain DN209 transformed with the vector pFG1.1, the pFG1.1 vector comprising a gene coding for a suppressor that is capable of suppressing the amber mutation in the DN209 strain, the transformed DN209 strain growing under conditions identical to those for the FA4-1-1 strain.

The metes and bounds of the term “consist essentially of” with regard to lactic acid bacterial DNA are not clearly defined in the specification (see the 112 2nd paragraph rejection above). The term can be interpreted broadly to encompass any recombinant vector comprising any sequences obtained directly from any lactic acid bacteria. It is further noted that applicants have not adequately described the structural/functional correlation required for a given vector to

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meet the functional limitations of the claims (see the 112 1st rejection for lack of written description above).

Claims 1-4, 7, 9-16, 22-24, 28-29, 31-33, 36 are rejected under 35 U.S.C. 102(b) as being anticipated by Dickely et al (applicants' submission A9; Dickely, et al. Molecular Microbiology, Vol. 15, No. 5, pages 839-847; see the entire reference).

Dickely et al teach the isolation and characterization of *L. lactis* nonsense suppressors and construction of a food-grade cloning vector utilizing one of the vectors. In particular, the authors describe the isolation and characterization of an amber or CUA suppressor (supD) from *Lactococcus lactis* (e.g. Abstract; Figure 3; page 841, column 2, second paragraph). In particular, expression vectors pAK89 and pAK89.1 are described that express the suppressor and demonstrate an ability to suppress an amber mutation in a selectable marker (Ery^R) in the *Lactococcus* strain MG1363 (page 841, columns 1-2, bridging paragraphs).

Given that the pAK89 and pAK89.1 are shown to grow in *Lactococcus* and function to suppress an amber mutation within a selectable marker gene, and given that applicants themselves have not adequately described what structural/functional correlation is required in order to meet the very specific functional limitations of the claims, one of skill in the art would necessarily expect that the expression vectors taught by Dickely et al meet at least one of the functional limitations of the claims (e.g. "essentially the same" rate of acidification in FH CY-1 as for the parental strain alone).

Because the Office does not have the facilities for examining and comparing the applicant's product with the products of the prior art, the burden is on the applicant to show a

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novel or unobvious difference between the claimed products and the products of the prior art (e.g. that the products of the prior art do not possess the same material structural and functional characteristics of the claimed product). See *in re Best*, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977).


Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Gerald G Leffers Jr., PhD whose telephone number is (571) 272-0772. The examiner can normally be reached on 9:30am-6:00pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Remy Yucel can be reached on (571) 272-0781. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).


GERY LEFFERS, PhD
PRIMARY EXAMINER
Primary Examiner
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SUGGESTION FOR DEPOSIT OF BIOLOGICAL MATERIAL
ATTACHMENT

A declaration by applicant or assignee, or a statement by applicant's agent identifying a deposit of biological material and averring the following may be sufficient to overcome an objection or rejection based on a lack of availability of biological material. Such a declaration:

1. Identifies declarant.
2. States that a deposit of the material has been made in a depository affording permanence of the deposit and ready accessibility thereto by the public if a patent is granted. The depository is to be identified by name and address. (See 37 C.F.R. § 1.803).
3. States that the deposited material has been accorded a specific (recited) accession number.
4. States that all restrictions on the availability to the public of the material so deposited will be irrevocably removed upon the granting of the patent. (See 37 C.F.R. § 1.808(a)(2)).
5. States that the material has been deposited under conditions that assure that access to the material will be available during the pendency of the patent application to one determined by the Commissioner to be entitled thereto under 37 C.F.R. § 1.14 and 35 U.S.C. § 122. (See 37 C.F.R. § 1.808(a)(1)).
6. States that the deposited material will be maintained with all the care necessary to keep it viable and uncontaminated for a period of at least five years after the most recent request for the furnishing of a sample of the deposited microorganism, and in any case, for a period of at least thirty (30) years after the date of deposit or for the enforceable life of the patent, whichever period is longer. See 37 C.F.R. § 1.806).
7. That he/she declares further that all statements made therein of his/her own knowledge are true and that all statements made on information and belief are believed to be true; and further, that these statements were made with knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the instant patent application or any patent issuing thereon.

Alternatively, it may be averred that deposited material has been accepted for deposit under the Budapest Treaty on the International Recognition of the Deposit of Microorganisms for the Purposes of Patent Procedure (e.g., see 961 OG 21, 1977) and that all restrictions on the availability to the public of the material so deposited will be irrevocably removed upon the granting of a patent.

Additionally, the deposit must be referred to in the body of the specification and be identified by deposit (accession) number, date of deposit, name and address of the depository, and the complete taxonomic description.